

CHOLECYSTOGRAPHY*

By R. G. VAN NUYS, M. D.
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DISCUSSION by C. G. Reynolds, M. D., Folsom; A. C. Siefert, M. D., Oakland; Fletcher B. Taylor, M. D., Oakland.

IN presenting this subject before a group of radiologists I shall be able to omit preliminary remarks, and shall refer to the literature only as it has direct bearing on the points I wish to emphasize.

ORAL ADMINISTRATION

We began to use cholecystography through oral administration of the Graham dye in June, 1925. This was given in various ways, viz.: pills, salol-coated capsules, a small capsule of dye placed in the larger capsule containing sodium bicarbonate, and finally in a specially prepared keratin-coated capsule. On reviewing the records of the first hundred cases examined by the oral method we find that about 50 per cent had symptoms of nausea, headache, and diarrhea. We soon realized that the tetraiodophenolphthalein when given by mouth is a gastro-intestinal irritant. Often there were undissolved pills or capsules in the colon, and when the hepatic flexure was high in hypersthenic individuals the dye shadows in the colon obscured the gall-bladder shadow. In the normal cases it was a great pleasure to visualize distinctly gall bladders on which before, we had to spend much time on exposure and much more time scrutinizing numbers of films from every angle. Blaine tersely says, "The percentage of correct diagnoses was formerly in direct proportion to the skill of the roentgenologist as a guesser."

INTRAVENOUS METHOD

There were certain of these oral cases where we found faint concentration which we determined to check by intravenous administration. We recall that the administration of salvarsan was once regarded as a hospital procedure, but that now this kind of intravenous medication is generally given in offices. We felt that if the method was to have general use it must be so modified that it could be used routinely in office practice, as many patients will not go to the hospital for such a procedure. We equipped our offices with adequate apparatus, with rest rooms, and hypodermics for combating the expected reactions. We soon found that no or very slight reactions were encountered and that many of the cases which were doubtful after oral administration of the Graham dye were much more definite and satisfactory of interpretation after intravenous injection. In over a hundred of these intravenous administrations in our offices, I have had only one untoward reaction of any consequence. This patient had previously had an unpleasant experience with capsules. She said to me as I gave the injection, "Why did you not give it this way before? It is much nicer." Just after I had withdrawn the needle the pulse quickened and she

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Figure 4
Plastic flap of ilium ready to be turned down. Method of reflection of capsule demonstrated.

Figure 5
Osteoplastic flap in femoral cleft.

articular hip fusion. By early fusion we are saving our patients years in getting well and also insuring against relapse.

I had the pleasure of seeing Doctor Wilson's patients recently at the American Orthopedic Association meeting, and the results are excellent.

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HAROLD H. HITCHCOCK, M. D. (1904 Franklin Street, Oakland)—I wish to thank Doctor Wilson for this method of extra-articular fusion of the hip which he has worked out. To me it is much more simple to do than the procedure of Doctor Hibbs. The more simple the procedure of fusing tuberculous joints becomes the more often it will be done, for fusion carries the only real assurance that these joints will stay healed.

The extra-articular method is certainly by all odds the best that has been produced, and again I wish to thank Doctor Wilson for having simplified that operation in the hip.

I would like to ask Doctor Wilson if he has much difficulty checking the bleeding from the ilium after having cut his graft and turned it down.

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DOCTOR WILSON (closing)—An extra-articular fusion would of course not be indicated unless a diagnosis of tuberculosis of the hip joint is unquestionable. Many of our cases have been subjected to animal inoculation of tissue from a suspected joint. Peri-articular tissue removed at the time of operation has shown positive microscopic and biologic evidence of tuberculosis in our cases.

In answer to Doctor Hitchcock's question concerning hemorrhage from the ilium I would say that there is no bleeding from either the flap or the denuded surface of the ilium which cannot be readily controlled with pressure.

New School of Speech-Reading in the West—Alhambra, California, has recently been added to the list of cities having classes of speech-reading in the evening public schools. Miss Marian J. Anderson, who has classes also at Monrovia and Inglewood, is in charge.—*Volta Review*.

became nauseated and vomited. The pulse, however, quickly returned to normal and the hypodermic was not necessary. She changed her mind; but this patient is the only one who has tried both and prefers the oral method. With this patient I was using 3 grams of the dye in 50 cc. of distilled water. After this experience I have been using 2.5 to 3 grams of the tetraiodophenolphthalein dissolved in 120 cc. of freshly doubly distilled water sterilized. The gravity method with physiological saline solution into the vein before and after the dye is used and occupies about twenty minutes for the injection of the dye proper. An evening meal containing some fat and protein, such as the meal suggested by Stewart: thick soup, creamed chicken, soft-boiled eggs, baked potatoes, bread and butter, and a glass of milk is recommended. The patient is given proper instructions and told to take a saline soda enema before retiring so that a thorough cleansing of the colon can be hoped for. Rigid fasting is insisted upon after the evening meal and until the patient reports at the office about nine the next morning. He is allowed to rest lying down for at least one-half hour after injection, and is then at liberty to go home and rest for four and one-half to five hours, when he returns for examination. If a satisfactory shadow of good concentration is obtained at this time, further concentrating time is not given, and he is asked to obtain a meal rich in fat. Two hours after he returns for further roentgen exposures. Tolysin, as suggested by Spurling and Hartman, was tried a dozen times with no marked difference in concentration noted. A few times we have given the dye before leaving the office at 6 p. m. and have let the patient fast until the morning hour. In other cases we have given the dye in the evening after dinner. With the latter methods the peak of concentration is reached, but since the method first outlined is satisfactory, there seems no reason to upset routine office hours. Practically all of our patients come for a complete gastro-intestinal study, and we feel that our work is incomplete if the gastro-intestinal examination does not immediately follow. This gives us an opportunity to observe for forty-eight hours the complete disappearance of the dye and to obtain indispensable gastro-intestinal evidence. We have tried in many cases, without success, to wash out the dye excreted from the liver by high enemata.

INTERPRETATION

Interpretation is often not difficult—the functions being either what we now consider normal or frankly pathological. By the latter we mean no, or faint, concentration after intravenous; calculi outlined; diverticulae; adhesions, etc. With McVicar, I feel that data should be collected with respect to two important facts:

1. Whether a diseased gall bladder may sometimes fill with opaque bile.
2. Whether the gall bladder which fails to fill is always so seriously diseased as to warrant its surgical removal.

He regards the most important limitation to

its clinical use the fact that in obstructive jaundice the opaque dye is not excreted.

Regarding the first question, I have been interested in those gall bladders which show fairly good concentration and contract very well but which appear rather flabby and often have a large cystic duct and which are found to retain the dye twenty-four, forty-eight, or even seventy-two hours after injection. I have films illustrating such a case which would seem to be pathological in spite of showing fair function. The reappearance of the gall-bladder shadow may be due either to delayed excretion or to reabsorption of the dye from the intestine. Where there is a normal concentrating time I feel that the reappearance of the shadow is due to reabsorption. Persistence of the shadow, however, to forty-eight hours and longer is probably pathological. I have come to feel that with our method, visualization of a gall bladder at twenty-four hours is the rule rather than the exception. I have not kept a record on all our intravenous cases, but in twenty-five recent cases which had fairly normal function I find over 80 per cent had a good gall-bladder shadow at twenty-four hours; about 50 per cent had a shadow still at thirty hours, and only a few are recorded as having a forty-eight hour retention. Two or three had a seventy-two hour retention. These observations will have to be checked up on many normals before their entire significance is appreciated. We have all seen fair function in gall bladders containing stones.

In regard to his second question, there are many who unhesitatingly affirm that the gall bladder which does not show normal concentration will not return to normal. Sherwood Moore in a recent article in the *Medical Journal and Record* says that we have "no reason to believe that pathological indications change to normal." He backs this observation by examination of excised gall bladders which he finds infected and feels that they could never return to normal. These observations bear much weight because they are based on a large number of cases examined by cholecystography, and also after operation. I feel that where there is no, or a faint, shadow on first examination, these cases should be checked, especially if the oral method is used. We have checked a few and found normal function after doubtful findings with the oral examination. We made one interesting observation on a female patient who had indefinite dyspeptic symptoms. Her gall bladder did not fill by what we regarded as a satisfactory oral administration. She faithfully carried out a medical régime for one year and the test was repeated again, using the oral method. She was feeling much improved in every way, and this time the cholecystograms showed normal function. I related this case to Sherwood Moore. He thought it possibly compatible with a diseased organ which recovered its function. Without the intravenous check following the first examination no conclusion can be drawn.

Regarding jaundice, which McVicar states is the most serious limitation to its clinical use, many writers have given jaundice as a contraindication. It is not a contraindication because of

obstruction. Copher found the toxicity increased only 25 per cent after ligating the common duct in dogs. The reason described by Graham, Moore and others, is that when the common duct is obstructed there is distention and increased tension and dilution of the bile with mucus. This increased tension does not allow the bile to enter the gall bladder. Sherwood Moore states that there is no need of the test in frank cases of cholecystic or biliary disease. Sydney Lang states that in jaundice the gall bladder never outlines with the dye regardless of the cause of the jaundice. As an exception to this last statement we had a case of an old lady with deep jaundice to whom we gave the dye orally. The gall bladder was outlined and numerous small, negative shadows were seen. The cystic duct could also be seen and was long and tortuous. At operation, the gall bladder as well as the common duct was found to contain stones. That the test is not necessary when there is frank cholecystitis, I shall cite the case of a man who had some jaundice plainly seen in his skin and sclera. The clinician strongly suspected biliary disease. Intravenous dye revealed normal function, and his jaundice was probably hemolytic in origin. According to McNee, jaundice may be caused by excessive hemolysis, toxic or infection action of the liver epithelium, the administration of certain drugs or obstruction of the bile passages. The dye then is often an aid in differentiating different types of jaundice.

As Graham has said this test is in its infancy, and as progress has been made with the barium meal, so it will be with this method. I think we should be on the alert to add any data which will increase its diagnostic accuracy. As it was necessary to examine a large number of healthy, young adults to fix a standard for the "position of the stomach, liver, and colon," so I feel that a series of normals should be examined to fix this standard for normal gall bladder interpretation. To this end I have started a series of gall-bladder examinations in the state prison of California where there are a large number of physically healthy adults of all ages. We have uncovered some very interesting findings in respect to blood pressure following the dye, but much more work will need to be done on this before any report can be made.

While I feel strongly that the intravenous method is generally preferable, I also feel that in some cases the oral method may be preferable. The clinician and the roentgenologist together can decide whether there are contraindications to the use of the intravenous. The final choice must often rest with the roentgenologist. If he finds a nervous, apprehensive patient with small veins, or with myocardial symptoms, it is usually better to try the oral method.

SUMMARY AND CONCLUSIONS

1. The Graham method of cholecystography has added greatly to our diagnostic accuracy, but the test is still in its infancy and further data will aid in clearing up some important questions.
2. The intravenous method of administration, if

carefully performed, is more dependable than the oral and is a safe office procedure.

3. The choice of method should in the last analysis rest with the thoughtful radiologist, whose duty it is to make this delicate test an indispensable adjunct to the clinician for the accurate diagnosis of gall-bladder disease.

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DISCUSSION

C. G. REYNOLDS, M.D. (State Prison, Folsom)—Doctor Van Nuys has covered the ground very thoroughly in discussing the merits of oral and intravenous methods of administering dye.

During the past eighteen months Dr. O. S. Cook of Sacramento and myself have been working up the relative merits between oral and intravenous administration, also the methods of oral administration. We have at present 150 patients that have had their complete series, both oral and intravenous, and seventy of these have come to operation.

I shall not include in my discussion those who have not come to operation.

We have found that there are fewer reactions with the plain gelatine capsule given with soda than when the keratin-coated capsule is used. We have had 32 per cent reactions in the oral administration, whereas with the intravenous administration we have had a little less than 2 per cent reactions.

After a light supper in the evening 3 grams of dye in capsules was given with soda at 9 o'clock at night. The patient fasted until the pictures were taken at 9 o'clock the next morning. Immediately following the picture a fatty meal was given; and an hour following the meal, another plate was taken to determine the amount of dye remaining in the gall bladder. The same routine was used when the dye was given intravenously, and Doctor Van Nuys's method of administration followed, except that we administered 3 grams of dye in double-distilled water, and did not wash the vein out with normal salt after the administration. We find this is less complicated, and have had only two cases in which there has been any sign of trouble. In these two cases the veins showed a brownish tinge at the site of injection which cleared up in a few weeks and at no time gave symptoms except discoloration. In the seventy cases, when our diagnosis was confirmed at the operating table, intravenous injection was found to be 34.4 per cent more efficient than the oral administration. We have also concluded that the intravenous method, as Doctor Van Nuys has suggested, is a safe office procedure, and less expensive than hospital procedure for the patient. At no time have we found that drugs were necessary to ward off the collapse or discomfort of a patient after intravenous administration.

The two facts that Doctor Van Nuys considers important: (1) "Whether a diseased gall bladder may sometimes fill with opaque bile; (2) whether the gall bladder which fails to fill is always so seriously diseased as to warrant its surgical removal," are very important.

We have had five cases that were completely jaundiced and still gave the shadows, the shadows not disappearing after the meals; two cases of a bile-filled gall bladder that contained stones which did not show on the plain film, the bladder emptying after the fatty meal in both instances; one case in which there were no stones on the plain film, no shadow on the film after oral administration, yet after the intravenous administration we found a well-defined shadow of the bladder at the fundic end of which was a well-outlined stone, confirmed at operation, the dye concentration about the periphery enhancing its borders enough to obtain a picture of it. The problem that must be further worked out which will greatly aid in settling the questions Doctor Van Nuys has raised is the physiology of the human gall bladder. I feel that cholecystography is a diagnostic aid for the radiologist that has not been perfected as yet. The physical examination and clinical findings are the

important factors in diagnosing early cholecystitis, in which cholecystography does not always reveal a diseased gall bladder. I feel sure this will be worked out as soon as the physiology and function of the gall bladder are fully determined.

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A. C. SIEFERT, M. D. (Merritt Hospital, Oakland)—The subject which Doctor Van Nuys has selected is one which never fails to draw an audience, though the number of papers published on cholecystography during the last three years in all civilized tongues is legion. Graham and his associates, like Lindbergh, have given us the realization of a dream which we all have dreamed. Reasonable certainty has taken the place of doubt in the roentgen diagnosis of gall-bladder pathology.

In this paper Doctor Van Nuys has covered the subject very completely, and Doctor Reynolds has so well supplemented his statements, that there is nothing left for me to say except to emphasize still further some of their points.

With me the intravenous method of administration of tetraiodophenolphthalein is the method of election. During the past twelve months I have used it to the exclusion of the oral method, and can base my statements on the experience gained from examination of 175 cases. In fully 33 per cent either no filling of the gall bladder was obtained or concentration was low. These 33 per cent would have yielded only equivocal results had the dye been administered orally.

The intravenous method in my hands has developed to a point where I consider it more safe and agreeable to the patient than the oral method. To be sure I still hospitalize my patients for convenience, but I no longer consider this essential.

Emphasis should be placed on the following details of technique:

1. The solution of the dye must be freshly prepared. It must not stand more than fifteen minutes before injection.

2. A dose of $2\frac{1}{2}$ grams is ample. I have found that the doses ordinarily recommended in the literature are too large, and a reaction, be it only a mild one, cannot be avoided.

3. The solution must be dilute. I use $2\frac{1}{2}$ grams of the dye dissolved in 100 cc. of normal saline solution. Greater concentration than this is not wise.

4. The dye must be administered slowly. The gravity method insures this better than injection by syringe. At least ten minutes should be allowed for injection, preferably more.

5. Pituitrin, surgical, 1 cc., administered hypodermically about one-half hour before injection of the dye, I have found to be efficient in preventing a fall in blood pressure to which the majority of the reaction symptoms are due. A contraindication to the use of pituitrin is a history of recent gall-stone colic. The drug does cause the gall bladder to contract and tend to empty itself as I have proven to my satisfaction by injecting it while cholecystography was in progress. Accordingly it will tend to force small calculi, if present, into the mouth of the cystic duct by causing gall-bladder contraction.

In the roentgenological examination proper I have found beside radiography fluoroscopy to be of value. If the gall bladder is visualized one can get considerable information by palpation concerning its mobility, elasticity, and sensitiveness.

As to interpretation of cholecystograms I, too, believe that the future will bring forth increasing accuracy in the early diagnosis of gall-bladder pathology. The basis, however, must be reliable routine of examination. The collection of a series of known normal cases on a large scale such as Doctor Van Nuys proposes to get will be of immense value.

I would like to record the following observations which I have made on my material. I am using the method of Newell for estimating the concentration of the dye in the gall bladder. With an injection of $2\frac{1}{2}$ grams of tetraiodophenolphthalein intravenously the concentration reaches its maximum at fifteen to

eighteen hours. With surprising frequency, I find that I estimate it at about 3 per cent in gall bladders against which no accusation of disease may be brought. In a few cases I have kept the gall bladder filled with dye containing bile for seventy-two hours by giving food absolutely free from fats. I have noticed no further concentration of the dye in such cases. These findings would lead me to say that $2\frac{1}{2}$ grams is an ample dose. No matter what the weight of the patient be the gall bladder will concentrate so much and no more, at least under ordinary conditions.

That the diseased gall bladder may and frequently does retain a considerable power of concentration, I think we all have experienced. That the converse is true, namely, that a gall bladder showing low concentrating ability is always diseased is not quite so certain. I have been reporting such cases as "presumptively pathological" pending further bioptic information.

Complete absence of filling, on the other hand, has in my experience always been more than adequately explained by findings at operation.

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FLETCHER B. TAYLOR, M. D. (1904 Franklin Street, Oakland)—The use of tetraiodophenolphthalein in outlining the gall bladder constitutes a definite help in the differential diagnosis of abdominal lesions. To regard it as more than a help is to invite inaccuracy and faulty clinical judgment. The negative, presumptive or positive findings from the method under consideration must serve as aids in diagnosis and not as pathognomonic or decisive items in determining a diagnosis and the subsequent therapy. If the patient is given the opportunity he will usually trace the disorders of function in himself by answering the questions of a carefully taken history. To put one's trust in mechanodiagnosis is as sterile a procedure as the chiropractor's wholesale mechanotherapy.

Unfortunately the patient has not the advantage of "local sign" in relating abdominal symptoms. He knows to the half inch where an injury has occurred in his somatic being because of the association of sight with sensation, and because of the completeness of his external sensorium. Some individuals seem to possess almost as efficient an internal reception as they have externally, but as a rule we need every bit of evidence obtainable to supplant the more usual lack of this power. The roentgen ray, laboratory findings and diagnostic surgical procedures here take their proper place, and clear visualization of the gall bladder is a welcome addition to the first of these.

It is wrong to suppose that normal gall bladders have a standard behavior or that pathological gall bladders will declare themselves without error just because we have a new way of looking at them. We must receive this with other additions to diagnostic procedure with judicial enthusiasm, interpreting the findings in the light of clinical observation in the individual patient.

A word might be added in regard to the route of administration. Should the dye be given directly into the blood stream, or indirectly by way of the alimentary canal? It is my impression that wherever possible we should avoid putting a foreign body directly into the blood stream. Practically I prefer the oral method for the general reason stated, to be followed by the direct intravenous route where results are indecisive.

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DOCTOR VAN NUYS (closing)—I wish to thank Reynolds, Siefert, and Taylor for their excellent discussions.

We will soon be able to obtain at a reasonable price the isomer of tetraiodophenolphthalein which, according to Sherwood Moore is less toxic, gives a denser shadow and slight persistence of the shadow. It will in addition give a test of liver function which will be used more generally as it becomes known. This substance will, I think, take away the objections to the intravenous method. As Bissell of Minneapolis

suggests, expediency seems to be the sole argument in favor of the oral method.

We have learned much by these methods, but we still have much to learn about cholecystitis. Most of the gall bladders examined by the pathologist will have some pathological change justifying our report of pathological gall bladder. We will be guided in our reports more and more by the effects experienced by the patients several years after the removal of what we term pathological gall bladders.

RHEUMATIC HEART DISEASE—FACTORS IN ITS PROGNOSIS*

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DISCUSSION by Harold K. Faber, M. D., San Francisco;
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I HAVE chosen the subject of prognosis in the rheumatic heart disorders of childhood, not because I consider myself an authority, but rather in order to point out the inadequacy of our common knowledge, and to suggest possible ways in which we may gain a greater insight into this perplexing problem.

INTRODUCTORY

In his lectures to the postgraduate students at the London Hospital, Sir James Mackenzie once remarked, "In your practice one question will arise incessantly and insistently implied or demanded of you by every patient, and that question is, 'What is to be the outcome of my complaint?' This question will meet you in most unexpected ways. Your diagnosis may be brilliant and yield you great satisfaction and the applause of your colleagues, but your patient will only be interested in it so far as it throws light upon his own future, and the problems thus presented are infinite."

No one can practice long without a forceful realization of the truth of this statement. Moreover if one has formed the habit of seeing things through the patient's eyes the reasonableness of the demand is obvious. Therefore most of us must find ourselves in agreement with Sir James Mackenzie when he says that "Prognosis is the coping stone which should complete the edifice of a medical education." But when and how is this last coping stone to be added to our educational edifice?

I venture to state that not one of us, while in medical school, ever received any clear-cut instruction on the prognostic significance of each abnormal symptom or sign in the cardiac disorders of childhood. And yet we are constantly confronted with young patients who present unusual irregularities, rate disturbances or murmurs. How can we predict the future wisely unless we do have some definite instruction in regard to the probable significance of such evidences of cardiac disorder?

When the physician is puzzled by unusual symptoms or signs he usually turns to some reference book—Osler, the loose-leaf systems, or a favorite textbook. There much knowledge may

be gained concerning the probable diagnosis and perhaps many useful, as well as useless, directions as to treatment. But alas, one looks in vain for definite advice which will enable one to give the patient a reliable prognosis. True it is considered the proper thing to insert a paragraph on this subject. But there are presented only vague generalities or else statistics on mortality or morbidity records in so many hundred cases with a given diagnosis. Such information does not help the physician to determine the probable outcome for his own particular patient nor to estimate the significance of individual subjective and objective phenomena.

We must confess, then, that there is great need for more data on the prognostic significance of all the various evidences of disturbed cardiac function. Furthermore there can be only one reliable method of obtaining the necessary information, and that is by the accurate observation of each patient from the onset of symptoms throughout the rest of the patient's life. There are few such observations available in the whole medical literature of the world and yet they would furnish us with invaluable information concerning prognosis. Nor should we forget that the practitioner is the man upon whom this burden must fall. He alone has the opportunity for the collection of these data, so necessary for the rounding out of our medical education.

The solution of this problem demands not only patient persistence and much time—a lifetime in fact—but also a thorough understanding of the closely allied subjects of diagnosis and treatment. Moreover in the very act of gaining a keener insight into prognosis one obtains information which is of great value in the diagnosis and treatment of the patient. This added knowledge may, in turn, enable the physician to alter the prognosis most favorably. I shall, then, consider briefly a few aspects of these subjects which seem to have a direct bearing on the prognosis.

DIAGNOSIS AS IT CONCERNS PROGNOSIS

It is not my purpose to attempt an evaluation of each symptom and sign of cardiac disturbance as to its prognostic significance. But I wish to call to your attention certain essential facts which we must bear in mind if we are to make any valuable contribution to the subject of "prognosis."

To say that we find positive signs of heart disease—or any other disease—usually means that the disease has advanced to the point of actual damage to the organ involved. Naturally the ideal toward which we strive is the prevention of disease or at least its arrest before any permanent damage has occurred. When I say that early diagnosis is of the utmost importance not only in the treatment but in the resulting prognosis I refer to a diagnosis which has been made before the heart is seriously damaged. For instance, we know that rheumatic arthritis, chorea, and such foci of infection as are represented by chronic tonsillitis or sinusitis, are the most frequent forerunners of carditis. Moreover its tendency to occur in several members of the same family suggests another causative factor. Therefore we must

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